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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/192,064	11/13/1998	HARTOUN HARTOUNIAN	07333/043001	9320
43517	7590	10/17/2005		
MASTERMIND IP LAW PC 421-A SANTA MARINA COURT ESCONDIDO, CA 92029			EXAMINER KISHORE, GOLLAMUDI S	
			ART UNIT	PAPER NUMBER

1615

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/192,064	Applicant(s) HARTOUNIAN ET AL.	
	Examiner Gollamudi S. Kishore, Ph.D	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12-35, 49, 51-53, 55-72 and 74-89 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 12-35, 49, 51-53, 55-72 and 74-89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

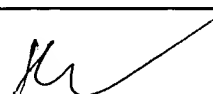
- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 July 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7-25-05</u> | 6) <input type="checkbox"/> Other: _____ |



DETAILED ACTION

The RCE dated 7-25-05 is acknowledged.

Claims included in the prosecution are 1-10, 12-35, 49, 51-53, 55-72 and 74-89.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 82 and 83 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim (cancer Treatment Reports, 1987) or Assil (arch. Ophthalmol. 1987) or Bonetti (Cancer Chemother. Pharmacol., 1994) or Kim (5,723,147), or Sankaram (5,766,627).

Kim, 1987, Assil, 1987, Bonetti 1994 or Kim 147 or Sankaram, 627 all teach multivesicular liposomes prepared by essentially similar process (Experimental sections in Kim 1987, Assil 1987, Bonetti 1994 and Examples in Kim 147 and Sankaram 627).

The burden is upon applicant to show that the instant product is patentably distinct from prior art product.

Claim Rejections - 35 U.S.C. ' 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

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subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1-10, 12-35, 49, 51-53, 55-72 and 74-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim (cancer Treatment Reports, 1987) or Assil (arch. Ophthalmol. 1987) or Bonetti (Cancer Chemother. Pharmacol., 1994) or Kim (5,723,147), or Sankaram (5,766,627) in view of Lenk (5,48,441), optionally in further combination with Bosworth (5,407,660).

The above references of Kim, 1987, Assil, 1987, Bonetti 1994 or Kim 147 or Sankaram, 627 all teach basically the same process of preparation of multivesicular liposomes.

The process involves dissolving the amphipathic lipid and the neutral lipid in chloroform and mixing it with an aqueous solution containing sucrose and forming an emulsion (instant step A), mixing this emulsion with an aqueous solution (step b) and removing the organic solvent and thereby forming the multivesicular liposomes (note the experimental sections in the publications and examples in Kim 147 and Sankaram 627).

What are lacking in these references are the teachings of filtration by cross-flow filtration method and making a sterile preparation.

Lenk while disclosing a method for size separation of particles teaches that there are problems associated with various methods previously available for the preparation

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of liposomes or vesicles of a select size and that by the cross-filtration method (also called as tangential flow filtration method) allows one to select large quantities of liposomes of a homogeneous, defined size distribution from a heterogeneously-sized population (note the abstract, col. 4, line 12 through col. 6, line 49). Lenk also discloses preparations for various modes of administration and sterile solutions (note col. 15, lines 1-19 and examples).

The use of cross-flow filtration step in the method of preparation of multivesicular lipid particles of Kim, Assil, Bonetti or Sankaram would have been obvious to one of ordinary skill in the art since Lenk teaches the advantages of using such a step in the preparation of vesicles or liposomes. It is deemed within the skill of the highly developed sciences to prepare a sterile preparation. It is also within the skill of the art to realize that if any composition is given by a systemic route, in the form of an injection in particular, that the preparation should be sterilized. Furthermore, it is clearly evident from Lenk that sterile preparations have to be used if they are administered to mammals. The criticality of the type of mixers and various method parameters recited in instant claims is not readily apparent to the examiner. In the absence of unexpected and unobvious results, these are deemed to be manipulations of the basic method steps by an artisan to obtain the best possible results. It is common practice in any field to perform a pilot method and extend it to a large-scale production. Similar is the case with the removal of the solvent using a two-step process sparging with different gas flow rates. Since Chloroform is toxic to animals and humans, it is within the skill of the art to recognize that this solvent has to be removed totally before the administration of the

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liposomes and therefore, one of ordinary skill in the art would flush the mixture with an inert gas such as nitrogen at different flow rates. That the Knowledge in the art of the removal of the organic solvent using a two step process to ensure that the organic solvent is totally removed is evident from the reference of Bosworth (Example 2).


5. In view of applicant's amendment to the claims removing the sterilizing step, the rejection of claims over Kim (cancer Treatment Reports, 1987) or Assil (arch. Ophthalmol. 1987) or Bonetti (Cancer Chemother. Pharmacol., 1994) or Kim (5,723,147) or Sankaram (5,766,627) in view of Lenk as set forth above, further in view of Kwasiborski (6,033,708), Fenski (5,837,282), Mehl (5,885,260), Castor (5,776,486), Moynihan (5,589,189) by themselves or in combination is withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK